

What is claimed is:

1. A method for preventing or treating a neoplasia disorder in a subject that is in need of such prevention or treatment comprising administering to the subject a topoisomerase I inhibitor and a Cox-2 selective inhibitor, wherein the topoisomerase I inhibitor is edotecarin.

2. The method according to claim 1, wherein the Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of celecoxib, parecoxib, deracoxib, valdecoxib, etoricoxib, meloxicam, rofecoxib, lumiracoxib, prodrugs of any of them, and mixtures thereof.

3. The method according to claim 1, wherein the Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of celecoxib, parecoxib, valdecoxib, and mixtures thereof.

4. The method according to claim 1, wherein the Cox-2 selective inhibitor is celecoxib.

5. The method according to claim 1, wherein the Cox-2 selective inhibitor comprises a chromene Cox-2 selective inhibitor.

6. The method according to claim 5, wherein the chromene Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of

6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,

7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphtho[2,1-b]pyran-3-carboxylic acid,
6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-

carboxylic acid,
6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-[(phenylmethyl)amino]sulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-(S)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,

6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic
acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid, and
mixtures thereof.

7. The method according to claim 5, wherein the chromene Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of

(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
(2S)-6,8-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-6-chloro-8-methyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-8-ethyl-6-(trifluoromethoxy)-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
and
(2S)-6-chloro-5,7-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid, and mixtures thereof.

8. The method according to claim 1, wherein the neoplasia disorder is at least one disorder selected from the group consisting of a neoplasia disorder of the lung, breast, skin, stomach, intestine, esophagus, bladder, head, neck, brain, cervix, and ovary.

9. The method according to claim 1, wherein the neoplasia disorder is at least one disorder selected from the group consisting of acral lentiginous melanoma, actinic keratosis, adenocarcinoma, adenoid cystic carcinoma, adenoma, adenosarcoma, adenosquamous carcinoma, astrocytic tumor, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinoma, capillary carcinoma, carcinoid, carcinoma, carcinosarcoma, cavernous carcinoma, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma, choroid plexus carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal carcinoma, epitheloid carcinoma, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumor, glioblastoma, glucagonoma, hemangioblastoma, hemangioendothelioma, hemangioma, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, interepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, a lentigo maligna melanoma, malignant melanoma, malignant mesothelial tumor, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillaryserous adenocarcinoma, pineal cell, pituitary tumor, plasmacytoma, pseudo sarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinoma, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor. ✓

10. A method for the prevention or treatment of topoisomerase I inhibitor-related diarrhea in a subject in need of such prevention or treatment wherein the method comprises administering to the subject a

diarrhea preventing or treating-effective amount of a source of a Cox-2 inhibitor, thereby preventing or treating the topoisomerase I inhibitor-related diarrhea, wherein the topoisomerase I inhibitor is edotecarin.

11. A therapeutic composition comprising a topoisomerase I inhibitor and a Cox-2 selective inhibitor, wherein the topoisomerase I inhibitor is edotecarin. 3

12. The therapeutic composition according to claim 11, wherein the Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of celecoxib, parecoxib, deracoxib, valdecoxib, etoricoxib, meloxicam, rofecoxib, lumiracoxib, prodrugs of any of them, and mixtures thereof.

13. The therapeutic composition according to claim 11, wherein the Cox-2 selective inhibitor is celecoxib.

14. The therapeutic composition according to claim 11, wherein the Cox-2 selective inhibitor comprises a chromene Cox-2 selective inhibitor.

15. The therapeutic composition according to claim 14, wherein the chromene Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of

6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphtho[2,1-b]pyran-3-carboxylic acid,
6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

8-chloro-6-[[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-(S)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,

6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic
acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid, and
mixtures thereof.

16. The therapeutic composition according to claim 14, wherein the
chromene Cox-2 selective inhibitor comprises at least one compound
selected from the group consisting of

(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-
carboxylic acid,
(2S)-6,8-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-6-chloro-8-methyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-8-ethyl-6-(trifluoromethoxy)-2-(trifluoromethyl)-2H-chromene-3-
carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
(2S)-6-chloro-5,7-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic
acid, and mixtures thereof.

17. A pharmaceutical composition comprising a topoisomerase I^a
inhibitor, a Cox-2 selective inhibitor, and a pharmaceutically acceptable
carrier, wherein the topoisomerase I inhibitor is edotecarin.

18. The pharmaceutical composition according to claim 17, wherein
the Cox-2 selective inhibitor at least one compound that is selected from
the group consisting of celecoxib, parecoxib, deracoxib, valdecoxib,

etoricoxib, meloxicam, rofecoxib, lumiracoxib, prodrugs of any of them, and mixtures thereof.

19. The pharmaceutical composition according to claim 17, wherein the Cox-2 selective inhibitor is celecoxib.

20. The pharmaceutical composition according to claim 17, wherein the Cox-2 selective inhibitor comprises a chromene Cox-2 selective inhibitor.

21. The pharmaceutical composition according to claim 20, wherein the chromene Cox-2 selective inhibitor comprises at least one compound selected from the group consisting of

6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid,
6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[(phenylmethyl) amino] sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic
acid,
6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-
carboxylic acid,
6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-6-[[(phenylmethyl) amino] sulfonyl]-2-trifluoromethyl-2H-1-
benzopyran-3-carboxylic acid,
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,

6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid,
5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,

6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid,
6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic
acid,
6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid, and
mixtures thereof.

22. The pharmaceutical composition according to claim 20, wherein
the chromene Cox-2 selective inhibitor comprises at least one compound
selected from the group consisting of

(S)-6-chloro-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-
carboxylic acid,
(2S)-6,8-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-6-chloro-8-methyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid,
(2S)-8-ethyl-6-(trifluoromethoxy)-2-(trifluoromethyl)-2H-chromene-3-
carboxylic acid,
(S)-6,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid,
(2S)-6-chloro-5,7-dimethyl-2-(trifluoromethyl)-2H-chromene-3-carboxylic
acid, and mixtures thereof.

23. A kit for preventing and treating neoplasia disorders in a subject
that is in need of such prevention and treatment, the kit comprising one
dosage form comprising a Cox-2 inhibitor and a second dosage form
comprising a topoisomerase I inhibitor, wherein the topoisomerase I
inhibitor is edotecarin.